

AMENDMENT

Amendments to the Claims

- Claim 1. (Currently amended) A method for selectively expressing a toxin within a cell comprising administering to the cell a DNA sequence comprising a promoter operatively linked to a transcription sequence; wherein the transcription sequence, when transcribed, produces a messenger RNA sequence that comprises a translatable sequence encoding a toxin, and an untranslated sequence; wherein the untranslated sequence inhibits translation of the toxin sequence under conditions that exist within normal mammalian cells that do not overexpress eukaryotic initiation factor eIF4E; wherein the untranslated sequence allows translation of the toxin sequence under conditions that exist within mammalian cells that overexpress eukaryotic initiation factor eIF4E relative to normal cells, and wherein the untranslated sequence further comprises a hairpin secondary structure conformation having a stability measured as folded state free energy of $\Delta G \leq$ about -50 Kcal/Mol.
- Claim 2. (Canceled)
- Claim 3. (Currently amended) The method of Claim [[2]] 1, wherein the administering is in an amount effective to inhibit cell growth.
- Claim 4. (Original) The method of Claim 3, wherein DNA sequence is administered by administering an expression vector encoding the DNA sequence to cells.
- Claim 5. (Original) The method of Claim 3, wherein the expression vector is delivered within a liposomal construct.
- Claim 6. (Original) The method of Claim 3, wherein the expression vector is delivered within a host cell.
- Claim 7. (Original) The method of Claim 3, wherein the expression vector is a viral vector.
- Claim 8. (Original) The method of Claim 3, wherein the expression vector is a non-viral vector.
- Claim 9. (Original) The method of Claim 3, wherein the expression vector is a BK vector.

Claim 10. (Original) The method of Claim 9, wherein the untranslated sequence allows translation of the toxin sequence under conditions that exist within mammalian cells that overexpress eukaryotic initiation factor eIF4E at least 2-fold greater relative to normal cells.

Claim 11. (Original) The method of Claim 10, wherein the encoded toxin is a conditional toxin.

Claim 12. (Original) The method of Claim 11, wherein the encoded conditional toxin is a herpes thymidine kinase.

Claim 13. (Currently Amended) A method for selectively expressing a toxin within a cell comprising administering to the cell a messenger RNA sequence that comprises a translatable sequence encoding a toxin, and an untranslated sequence; wherein the untranslated sequence inhibits translation of the toxin sequence under conditions that exist within normal mammalian cells that do not overexpress eukaryotic initiation factor eIF4E and wherein the untranslated sequence allows translation of the toxin sequence under conditions that exist within mammalian cells that overexpress eukaryotic initiation factor eIF4E relative to normal cells, wherein the untranslated sequence comprises an mRNA sequence with a secondary structure conformation having a stability measured as folded state free energy of $\Delta G \leq$ about -50 Kcal/Mol.

Claim 14. (Canceled)

Claim 15. (Currently amended) The method of Claim [[14]] 13, wherein the administering is in an amount effective to inhibit cell growth.

Claim 16. (Previously presented) The method of Claim 13, wherein the step of administering to the cell a messenger RNA sequence comprises administering an expression vector to the cell wherein the expression vector produces the messenger RNA sequence in situ and thereby administers the messenger RNA to the cell.

Claim 17. (Original) The method of Claim 16, wherein the expression vector encodes a DNA sequence encoding the messenger RNA sequence.

Claim 18. (Original) The method of Claim 17, wherein the expression vector is delivered within a liposomal construct.

Claim 19. (Original) The method of Claim 17, wherein the expression vector is delivered within a host cell.

Claim 20. (Original) The method of Claim 17, wherein the expression vector is a viral vector.

Claim 21. (Original) The method of Claim 17, wherein the expression vector is a non-viral vector.

Claim 22. (Original) The method of Claim 17, wherein the expression vector is a BK vector.

Claim 23. (Original) The method of Claim 17, wherein the encoded toxin is a conditional toxin.

Claim 24. (Original) The method of Claim 17, wherein the encoded conditional toxin is a herpes thymidine kinase.

Claim 25. (Currently amended) A method of treatment for cancer in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of a DNA sequence comprising a promoter operatively linked to a transcription sequence; wherein the transcription sequence, when transcribed, produces a messenger RNA sequence that comprises a translatable sequence encoding a toxin, and an untranslated sequence; wherein the untranslated sequence inhibits translation of the toxin sequence under conditions that exist within normal mammalian cells that do not overexpress eukaryotic initiation factor eIF4E; and wherein the untranslated sequence allows translation of the toxin sequence under conditions that exist within tumor cells that overexpress eukaryotic initiation factor eIF4E relative to normal cells, wherein the untranslated sequence further comprises a hairpin secondary structure conformation having a stability measured as folded state free energy of $\Delta G \leq$ about -50 Kcal/Mol.

Claim 26. (Canceled)

Claim 27. (Currently amended) The method of Claim ~~[[26]]~~ 25, wherein DNA sequence is administered by administering an expression vector encoding the DNA sequence to the mammal.

Claim 28. (Original) The method of Claim 27, wherein the expression vector is delivered within a liposomal construct.

Claim 29. (Original) The method of Claim 27, wherein the expression vector is delivered within a host cell.

Claim 30. (Original) The method of Claim 27, wherein the expression vector is a viral vector.

Claim 31. (Original) The method of Claim 27, wherein the expression vector is a non-viral vector.

Claim 32. (Original) The method of Claim 27 wherein the expression vector is a BK vector.

- Claim 33. (Original) The method of Claim 27, wherein the untranslated sequence allows translation of the toxin sequence under conditions that exist within tumor cells that overexpress eukaryotic initiation factor eIF4E at least 2-fold greater relative to normal cells.
- Claim 34. (Original) The method of Claim 27, wherein the untranslated sequence allows translation of the toxin sequence within tumor cells in which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the toxin is translated to kill the tumor cells.
- Claim 35. (Original) The method of Claim 34, wherein the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eIF4E typically present in non-tumor cells
- Claim 36. (Original) The method of Claim 35, wherein the encoded toxin is a conditional toxin.
- Claim 37. (Original) The method of Claim 36, wherein the encoded conditional toxin is a herpes thymidine kinase; and wherein the method additionally comprises administering an effective amount of ganciclovir to the mammal.
- Claim 38. (Original) The method of Claim 37, wherein the cancer is a metastatic tumor.
- Claim 39. (Original) The method of Claim 37, wherein the cancer is a solid tumor.
- Claim 40. (Original) The method of Claim 38, wherein the metastatic tumor is associated with a mammalian cancer selected from the group consisting of bladder, breast, cervical, colon, lung, prostate, and head and neck.
- Claim 41. (Currently amended) A method of treatment for cancer in a mammal, comprising administering to a mammal in need of such treatment a therapeutically effective amount of a messenger RNA sequence that comprises a translatable sequence encoding a toxin, and an untranslated sequence; wherein the untranslated sequence inhibits translation of the toxin sequence under conditions that exist within normal mammalian cells that do not overexpress eukaryotic initiation factor eIF4E and wherein the untranslated sequence allows translation of the toxin sequence under conditions that exist within mammalian cells that overexpress eukaryotic initiation factor eIF4E relative to normal cells, wherein the untranslated sequence further comprises a hairpin secondary structure conformation having a stability measured as folded state free energy of $[[AG]] \Delta G \leq \text{about } -50 \text{ Kcal/Mol}$.

Claim 42. (Canceled)

Claim 43. (Currently amended) The method of Claim ~~[[42]]~~ 41, wherein the step of administering to the cell a messenger RNA sequence comprises administering an expression vector to the cell wherein the expression vector produces the messenger RNA sequence in situ and thereby administers the messenger RNA to the cell.

Claim 44. (Original) The method of Claim 43, wherein the expression vector encodes a DNA sequence encoding the messenger RNA sequence.

Claim 45. (Original) The method of Claim 44, wherein the expression vector is delivered within a liposomal construct.

Claim 46. (Original) The method of Claim 44, wherein the expression vector is delivered within a host cell.

Claim 47. (Original) The method of Claim 44, wherein the expression vector is a viral vector.

Claim 48. (Original) The method of Claim 44, wherein the expression vector is a non-viral vector.

Claim 49. (Original) The method of Claim 44, wherein the expression vector is a BK vector.

Claim 50. (Original) The method of Claim 44, wherein the untranslated sequence allows translation of the toxin sequence within tumor cells in which the presence of eukaryotic initiation factor eIF4E allows the translation of the toxin, the toxin is translated to kill the tumor cells.

Claim 51. (Original) The method of Claim 50, wherein the majority of non-tumor cells in the mammal are not killed due to the low levels of eukaryotic initiation factor eEF4E typically present in non-tumor cells

Claim 52. (Original) The method of Claim 51, wherein the encoded toxin is a conditional toxin.

Claim 53. (Original) The method of Claim 52, wherein the encoded conditional toxin is a herpes thymidine kinase; and wherein the method additionally comprises administering an effective amount of ganciclovir to the mammal.

Claim 54. (Original) The method of Claim 53, wherein the cancer is a metastatic tumor.

Claim 55. (Original) The method of Claim 53, wherein the cancer is a solid tumor.

Claim 56. (Original) The method of Claim 54, wherein the metastatic tumor is associated with a mammalian cancer selected from the group consisting of bladder, breast, cervical, colon, lung, prostate, and head and neck.